DENTAL PRODUCTS

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INTRODUCTION

A considerable number of products are now recommended for use in the oral cavity. Products for caries control are widely used and include fluorides in dentifrices and mouthwashes. Plaque control is achieved through the use of chemical agents such as chlorhexidine and quaternary ammonium compounds. Mechanical products for plaque control include dental floss, toothpastes, and mouthwashes. Products also exist to combat halitosis, act as topical anesthetics, desensitize sensitive teeth, act as tooth-bleaching agents, and assist in reducing xerostomia. More recently, products designed for the local delivery of antimicrobial agents to the oral cavity have also been made available. These, and other products, are reviewed in this article.

CARIES CONTROL USING FLUORIDES

Over 300 million people worldwide now consume optimally fluoridated water. The U.S. Public Health Service has established recommended levels for fluoride concentrations in water supplies in accordance with mean annual temperatures (1). The daily intake of fluoride not only comes from drinking water but also from food consumed or prepared with fluoridated water. Also, crops are frequently fertilized with phosphate fertilizers of high soluble-fluoride content, and food products including bone in animal feeds contain fluoride.

Naturally fluoridated foods and water have been ingested for decades with no serious side effects. In addition, public fluoridation has been widespread in this country for over 30 years without serious adverse effects. The incidence of mottled enamel, one of the earliest and most sensitive signs of fluoride toxicity, has not increased significantly in the past 15 years of water fluoridation. The safety and efficacy of fluoride has definitely been established, with no scientific evidence against fluoridation.

Mechanism of Action

The mechanism by which fluoride prevents caries is not clearly understood. It is known that the fluoride ion (F^-) can replace the hydroxyl ion (OH^-) in hydroxyapatite, the major crystalline structure of enamel. The substituted crystal, called fluorapatite, is more resistant to acids, such as those produced by plaque bacteria, than the original hydroxyapatite.

As the tooth develops and enamel is formed, ingested fluoride is incorporated into the enamel. Therefore, because enamel develops its outer layer first, more fluoride can be expected to be deposited on the outer layers as compared to the inner layers. It is this surface enamel layer containing fluoride that imports, in part, caries resistance to a tooth (2). Topical fluorides also become incorporated into enamel and provide protection against acid. A number of studies have now shown that topical fluorides may be most beneficial in early enamel caries and that there is an increased uptake of fluoride in early lesions, with some tooth remineralization occurring. This finding has caused some investigators to label fluoride as a remineralizing agent as well as a caries inhibitor. The incorporation of fluoride into enamel can be represented as a chemical reaction:

$$Ca_{10}(PO_4)_6(OH)_2 + F \rightarrow Ca_{10}(PO_4)_6F_2 + 2(OH)^-$$

Dental plaque also tends to concentrate fluoride. This could increase possible antienzymatic activity. Some caries protection from this may be expected. Additionally, studies have suggested that topical application of fluoride may also reduce smooth surface plaque, with a resulting beneficial effect on the periodontal tissues (3).

In areas where there is no fluoridation of the community water supply, fluoride may be added to school water. This is not a substitute for community water fluoridation because fluoride intake from birth is important.

In some areas where fluoride is absent from drinking water, the school water supply has been fluoridated as much as 4.5 times the level usually recommended for community water levels. These studies, conducted for 12 years in fluoride-deficient areas, revealed a 40% reduction in DMF surfaces. Essentially, no undesirable fluorosis resulted from this procedure. However, it should be noted that ingestion occurred only during part of each day and only on school days. This level (4.5 ppm) from birth (during major formation of permanent teeth) would cause undesirable fluorosis with continued intake (4).

Therapeutic Effects

Fluoridated water

The administration of fluoride in drinking water at concentrations of approximately 1 ppm significantly reduces dental caries. The anticaries benefits are similar to those due to natural fluoride in drinking water. Fluoridated drinking water produces the following: a 60% lower dental caries rate, a 75% decrease in the loss of 6-year molars, and a 90% reduction in the incidence of proximal caries of the four upper anterior teeth.

Evidence suggests that greater inhibition of caries occurs when teeth receive fluoride throughout the calcification period. Therefore, maximum benefit may be expected from the continued use of fluoridated drinking water.

Dietary supplements/tablets

Maximum benefits to both deciduous and permanent teeth may result from daily fluoride supplements from infancy until approximately 13 years of age, at which time all permanent teeth except the third molars should have erupted. Because cariostatic benefits may tend to diminish gradually after fluorides are discontinued, periodic applications of topical fluorides may then be necessary.

The use of dietary fluoride or topical applications of fluoride depends partly on the age of the child. Dietary supplements of fluoride are best for very young children, whereas topical fluoride applications are preferred for older children with permanent teeth. Younger children who are highly susceptible to caries may benefit from both measures.

The natural level of fluoride in drinking water where the child lives should be known before dietary fluoride is prescribed. At present, it is suggested that fluoride supplements be limited to where drinking water contains 60% or less of the optimal level of fluorides recommended for community water in the geographic area.

As a precaution, no large quantities of sodium fluoride should be stored in the home. It is recommended that no more than 264 mg of sodium fluoride be dispensed at any one time, which is enough for at least a 4-month period (5). Each package dispensed should also bear the statement: Caution—store out of the reach of children.

Although the optimal level of fluoride in drinking water is well documented, there is no established allowance for fluoride administered once a day. The standard allowance is 1 mg/day for a child over 3 years of age and one-half this amount for a child between the ages of 2 and 3. A more accurate method to use in calculating the daily fluoride needs of a child is to administer a dose based on the child's weight, for example, .025 mg/lb of body weight. However, for all children over 6 months of age, the dose should not exceed 1 mg/day of fluoride ion regardless of weight. In order to avoid the possibility of unesthetic dental fluorosis, the prescribed dietary allowance should be reduced in proportion to the fluoride levels in the drinking water. Table 1 illustrates empirical adjustments for varying amounts of natural fluorides in communities where the recommended optimal level of fluoride is 1 ppm. These allowances are for children over 6 years of age. The allowances should be reduced for children 6 years of age and under, as shown in Table 2 (6, 7).

Table 1 Adjustment of prescribed fluoride relative to natural content of drinking water for children over 6 years of age

Water fluoride (ppm[a])	Adjusted allowance sodium fluoride (mg/day)	Provides fluoride ion (mg/day)
0.0	2.2	1.0
0.2	1.8	0.8
0.4	1.3	0.5
0.6	0.0	0.0

[a]1 ppm = 1 mg/L.

For children under 6 months of age, experts question the value of prescribing fluoride supplements.

Dental caries have been prevented when fluoride tablets were administered in a school-based program. After two or more years of fluoride ingestion, protection against dental caries ranged from 20–40% (8). In an extended trial of fluoride tablets reported in the literature, there was a 36% reduction in dental caries after 8 years (9).

The use of fluoride tablets can provide both a preeruptive (endogenous) effect and a posteruptive (topical) effect. Therefore, tablets should be chewed or dissolved in the mouth and the teeth rinsed with the resultant solution before swallowing.

One advantage of fluoride tablets compared to water fluoridation is that a specific dosage of fluoride is delivered.

Table 2 Adjustment of prescribed fluoride ion relative to natural content of drinking water for children under 6 yr of age

	Content of water fluoride[a]		
Patient's age	0–0.3 ppm	0.3–0.6 ppm	>0.6 ppm
0–6 mon	0.0	0.0	0.0
6 mon–3 yr	0.25	0.0	0.0
3–6 yr	0.50	0.25	0.0

[a]2.2 mg prescribed sodium fluoride = 1 mg fluoride ion.

One disadvantage is that dietary supplements of fluoride taken once a day are rapidly cleared from the body.

Breast-feeding

Fluoride levels in human breast milk have been found to be less than 0.05 ppm. This concentration remains constant, regardless of drinking water and maternal plasma levels. Thus, breast-fed infants who receive no formula bottle feedings ingest considerably less fluoride than infants receiving formula mixed in 1 ppm fluoridated water. Fluoride supplementation for breast-fed infants should be considered.

The administration of fluoride supplements to expectant mothers in an effort to benefit the teeth of the offspring has been evaluated in several studies (10, 11). The evidence, however, is not sufficiently conclusive to warrant recommendation.

Vitamins

Vitamin preparations containing sodium fluoride are also available as drops, tablets, and chewable tablets. These forms of supplementation are useful in areas where the water supply contains less than 0.6 ppm, and they offer a way to provide fluoride to the child, if the parents are conscientious in dispensing the required amount daily and if the child does not object to taking oral medications. In recommending vitamins with fluoride, it is mandatory that one know the fluoride content of the child's water supply, as well as the fluoride content of the vitamin being recommended.

Topicals

Fluoride can be applied topically in various forms, offering the practitioner a number of options to choose for his or her patients.

Topical agents are of lesser value in a caries reduction program when they are used in fluoridated communities. However, when used in nonfluoridated areas, they are more effective (12, 13). In such areas, they often are the only form of fluoride therapy available.

The dosage forms of topical fluoride currently available include varnishes, dentifrices, solutions, gels, mouthwashes, and prophylaxis pastes. These various forms are outlined in Table 3.

Dentifrices

The earliest fluoride dentifrices contained sodium fluoride. However, the fluoride was biologically unavailable because the calcium in the dentifrice abrasive bound the fluoride and thus inactivated it.

Although a number of dentifrices containing fluoride are on the market, not all provide available fluoride because the abrasive systems that some dentifrices contain inactivate the fluoride. Therefore, the product may contain as much fluoride as any other dentifrice but it is not available. Also, if the product has a short shelf life, it will be ineffective if poor marketing gets it to the consumer too late.

For these reasons, only dentifrices approved by the Council on Scientific Affairs of the American Dental Association (ADA) should be recommended. These

Table 3 Various topical fluoride preparations

Preparation	Form	Formulation
Acidulated phosphate fluoride	Topical solution	1.23% in 1% phosphoric acid
	Topical gel, foam	1.23% in 1% phosphoric acid
	Mouthrinse	0.02–0.04%
	Prophylaxis paste	1.2%
Amine fluoride	Dentifrice	1.6%
	Mouthrinse	2.5%
Sodium fluoride	Topical solution	2%
	Mouthrinse	2.5%
	Foam	0.2%
	Varnish	5% (every 3–6 months)
Sodium monofluorophosphate	Dentifrice	0.76–0.8%
Stannous fluoride	Topical solution	8%
	Mouthrinse	0.1%
	Prophylaxis paste	8%
	Dentifrice	0.4%
	Gel	0.4%

Table 4 Representative dentifrice ingredients

Brand name	Fluoride	Abrasive	Sweetener
Aim	0.8% Sodium MFP	10% hydrated silica xerogel 19% hydrated silica	67% Sorbitol
Aim extra strength	1.2% Sodium MFP		
Aquafresh	0.76% Sodium MFP	12.6% Calcium carbonate 12% Silica	52.8%
Colgate®	0.76% Sodium MFP	48.76 Dicalcium phosphate	22% Glycerin
Crest®	0.24% Sodium fluoride	20% Hydrated silica	50% Sorbitol 18% Glycerin
Macleans	0.76% Sodium MFP	38% Calcium carbonate	29.55% Glycerin

products are listed in that association's publications and carry the ADA seal on their packaging.

Currently accepted dentifrices contain sodium monofluorophosphate, sodium fluoride, or, less frequently, stannous fluoride, all of which reduce caries by approximately 25% when used daily. In some clinical studies, stannous fluoride dentifrices stained teeth, particularly in pits and fissures (14). This stain is related to the tin in this compound, which adheres to plaque. The significance of this staining and its esthetic problems have resulted in a decreased usage in dentifrices. Stannous fluoride dentifrices are marketed in a plastic container because a reaction of stannous ions at an acid pH occurs when conventional soft metal tubes are used.

The composition of some popular toothpastes is important for a proper understanding of this topic. With the exception of extra strength products, the various dentifrices are formulated to provide 1000 ppm of fluoride. Comparative compositions of some fluoride dentifrices are shown in Table 4.

Since children ingest most of the fluoride toothpaste when they brush their teeth, only a pea-sized amount should be placed on the brush.

Stannous fluoride

Dentifrices containing stannous fluoride as an active ingredient are no longer widely marketed; however, these formulations were the first to be evaluated for caries-reducing properties. Effectiveness in caries reduction varied from 23 to 34% (15, 16). One stannous fluoride dentifrice containing a patented stabilized form of stannous fluoride is marketed with a claim of both caries and gingivitis reduction. However, this product is not ADA accepted.

Currently, there are no ADA-approved, over-the-counter dentifrices containing stannous fluoride. However, there are a number of ADA accepted stannous fluoride prescription products approved for application by the dentist or by the patient.

Amine fluoride

Clinical data from several long-term studies in Europe have demonstrated the effectiveness of the use of a dentifrice containing organic amine fluorides (17, 18). The amine fluorides also have strong plaque-reducing properties. However, although the amine fluorides may be more effective for caries reduction than other forms of fluoride, the FDA has not allowed these products to be extensively tested in this country.

Sodium fluoride

Sodium fluoride as an ingredient in dentifrices has been the subject of a number of clinical investigations. Recent studies of sodium fluoride dentifrices formulated to ensure ready availability of fluoride ions have shown anticaries benefits similar to those obtained in clinical caries trials with dentifrices containing stannous fluoride and sodium monofluorophosphate.

Clinical caries trials conducted under well-controlled, daily supervised brushing conditions have reported reductions in dental caries of approximately 25–48% (19, 20).

Sodium monofluorophosphate

A number of clinical studies have been conducted with dentifrices containing 0.76% monofluorophosphate (MFP). The data from these controlled clinical studies of sodium MFP dentifrices have indicated reductions in dental caries ranging from approximately 17–42% (21–23). Two studies indicating effectiveness were conducted in fluoridated communities. In clinical studies comparing this form of fluoride with sodium fluoride, the findings for caries reduction have been similar. Unlike dentifrices containing sodium fluoride, dentifrices

containing MFP are compatible with a number of abrasive systems; this is one of the reasons why there are more ADA-accepted products in this category.

Solutions and Gels

In children, a reduction of 30–40% in dental caries is seen with the following: 2% sodium fluoride, 8% stannous fluoride, and acidulated phosphate-fluoride products. No one agent appears to be superior to any other when used as directed.

Solutions of 8% stannous fluoride have been used to reduce caries (24). As with the other agents, the teeth are polished, dried, and isolated, and a 4-min application follows. The disadvantages of this solution are that it must be freshly prepared, some tooth discoloration (as discussed under dentifrices) has occurred, and it has an unpleasant taste that is difficult to mask.

Topical concentrated fluoride solutions are useful in children with high caries activity because they may have both a caries-arresting property and one of caries prevention. The frequency of application varies with the caries activity of the child. For children with an average incidence of caries, it can be applied annually between the ages of 3 and 13.

When gels are used, they are placed into a tray that is placed against the teeth so that the gel flows around all surfaces. Best results have been reported with custom-fitted trays. It has been estimated that about one-third of the total fluoride placed in a tray is actually available for uptake by teeth. The remainder is simply a filler for the tray, some of which is swallowed (25).

The value of topical fluorides on adults has not been established. However, some studies have suggested that the acidulated phosphate fluoride types may offer some caries protection. Recent reports have suggested that polishing of teeth is not necessary prior to the topical application of fluorides (26, 27). These studies have stated that deplaquing of teeth with a toothbrush is adequate and offers the advantage of not removing surface fluoride from tooth structure. This concept may be valid, and future investigations in this area should be encouraged.

Fluoride mouthwashes

Substantial research has been performed on the caries-inhibiting effect of fluoride mouthrinse products. The effectiveness of these topically applied fluorides varies with patient compliance.

The daily use of fluoride rinses by young children should be carefully monitored, and it should be noted that the ADA does not recommend the use of fluoride mouthrinse for children under 6 years of age.

Moreover, because these products, when brought into the home, present a potential danger, the ADA Council on Scientific Affairs has recommended that these rinses should not exceed 300 mg of sodium fluoride. Fluoride mouthrinse solutions for use in school or community programs, however, are available in larger volumes, based on the assumption that storing and dispensing of the products in public settings will be closely monitored. The potential dangers involved with unsupervised ingestion of these products should be made known to both parents and children.

Studies evaluating the effectiveness of mouthrinses containing sodium fluoride have shown the usefulness of these agents for children living in nonfluoridated areas. Most studies have been conducted using a mouthrinse containing approximately 0.05% sodium fluoride used daily or a 0.2% sodium fluoride used weekly (28, 29).

The Council on Scientific Affairs has accepted a number of fluoride mouthrinses. All products discussed below have ADA Council on Scientific Affairs acceptance.

Some mouthrinses are marketed as a concentrate for dilution to recommended levels. If concentrates are used, special care should be exercised to keep them out of the reach of children. The products are not packaged in glass containers, because the pH becomes more alkaline in glass. Plastic is the container of choice. Examples of prescription and nonprescription products follow.

ACT

This product is an aqueous solution of 0.05% sodium fluoride. It also contains 8% glycerin, 7% alcohol, a detergent, a preservative, saccharin, coloring, and flavoring agents. It is intended to be used on a daily basis and is available without prescription.

Fluorigard

This product is available as a rinse containing an aqueous solution of a 0.05% sodium fluoride, 15% glycerin, 5% alcohol, a detergent, a preservative, saccharin, coloring, and flavoring agents. It is intended to be used on a daily basis and is available without a prescription.

Fluorinse

This product contains 0.2% sodium fluoride as the active ingredient. It also contains a detergent, a preservative, flavoring, and color agents. It is intended to be used on a daily basis and is available without a prescription.

Phos-Flur oral rinse supplement

This product is an aqueous solution containing 0.044% sodium fluoride, 0.055%, phosphoric acid, 1.35% sodium biphosphate, and flavoring and coloring agents. It is intended to be used once daily and is available by prescription.

Desensitizing Agents

A number of studies have reported that topical fluoride application may reduce dental hypersensitivity (30–32). These results have been found when concentrated dosage forms have been applied ranging from 8% stannous fluoride gels to 33.3% sodium fluoride paste. It has been shown that commercial dentifrices containing stannous fluoride may also decrease dental hypersensitivity. Also, a combination of stannous fluoride and potassium nitrate is marketed by one manufacturer to reduce sensitivity. Varnishes containing sodium fluoride have also been shown to reduce dental hypersensitivity.

CHEMICAL AGENTS FOR PLAQUE CONTROL

A number of chemical agents have been evaluated over the years in terms of their antimicrobial effects in the oral cavity and the importance of these effects on oral health.

In 1986, the establishment by the ADA of guidelines for acceptance of these products has served to stimulate properly designed clinical studies for evaluating potential therapeutic agents. Products that have earned the ADA's seal of acceptance are Peridex, Listerine®, some generic copies of Listerine, and Colgate Total®.

In this section, data on various available agents are presented according to chemical agent category. When the term *substantivity* is used, it refers to the ability of an agent to be retained in the area cavity and to be released over an extended time period with a continued antimicrobial effect.

Chlorhexidine

Of the products included in this report, chlorhexidine appears to be the most effective agent. Long-term studies in over 700 subjects showed reductions in plaque averaging 55% and in gingivitis 45% (33–35).

The mechanism of action of chlorhexidine is related to a reduction in pellicle formation, alteration of bacterial absorption and/or attachment to teeth, and an alteration of the bacterial cell wall so that lysis occurs. Chemically, it is classified as chlorhexidine digluconate and the U.S. Adopted Name (USAN) designation is chlorhexidine gluconate. It has high substantivity. Adverse effects reported included staining of teeth, reversible desquamation in young children, alteration of taste, and an increase in supragingival calcified deposits. Long-term and microbiologic studies do not demonstrate the development of resistant strains. It is sold in the United States in a 0.12% concentration as a prescription mouthrinse (Peridex, PerioGard, and generically), which contain 11.6% alcohol with a pH of 5.5 and is approved by the ADA for control of plaque and gingivitis. Recommended usage is twice daily.

Fluorides

Fluorides are purported to have some antiplaque properties. The most widely used topical fluorides are stannous fluoride, acidulated phosphate fluoride, and sodium fluoride. Of the fluorides, short-term studies of stannous fluoride have been promising. However, long-term published studies showed lower plaque scores, but the differences were not significant (36, 37). No effect on gingival health was noted with the exception of one study.

With stannous fluoride, the mechanism of action appears to be related to an alteration of bacterial aggregation and metabolism. In summarizing the properties of this agent, it can be stated that it has moderate substantivity, that the antibacterial activity may be related to the tin ion, and that a 0.4% concentration may be the most effective. Stannous fluoride is the most toxic of the products considered and has the shortest shelf life. Adverse effects have been taste and black stain lines on teeth. Usage of once or twice daily favors compliance. Stannous fluoride is most often available as an aqueous gel.

Stannous fluoride products are accepted by the ADA for their ability to deliver fluoride but have not been approved for their plaque-reducing properties. Examples of accepted products are Activux Basic Control, Gel-Kam, Gel-Tin, Perfect Choice, Pro-Dentx, Schein Home Care, and Super-Dent.

Oxygenating Agents

In evaluating the efficacy of oxygenating agents, one must evaluate the endpoints selected for efficacy and their measurement. Oxygenating agents have anti-inflammatory properties. Therefore, less bleeding on probing, a major sign of inflammation, would be expected following their use, but the bacteria producing the disease process would not necessarily have been reduced. Peroxides are found in dentifrices in combinations with sodium bicarbonate in

concentrations of 1.5% or less. Also, they are found in bleaching agents discussed later in this chapter. As long-term studies of the effect of oxygenating agents are unavailable and short-term studies offer contradictory findings, questions of safety have been raised with regard to chronic use (38, 39).

Phenolic Compounds

Listerine

Short-term studies of phenolic compounds have shown plaque and gingivitis reductions averaging 35%, and long-term studies have shown plaque reduction averaging 35% and gingivitis reduction averaging 30% (40–42).

The only product in this category that has been adequately studied is Listerine. Listerine is a mixture of essential oils—thymol, menthol, a eucalyptol, and methylsalicylate. The mechanism of action appears to be related to alteration of the bacterial cell wall. This product is uncharged and has a low substantivity. Adverse effects reported have been a burning sensation and bitter taste. It is available in a 21.6–26.9% alcohol vehicle with a pH of 4.2. Recommended usage is twice daily, and the ADA accepts the product and some of its generic copies for the control of plaque and gingivitis.

Plax

Only short-term, clinical studies with small numbers of patients have been published. These pilot studies suggested some reduction in plaque when this product was used as a prebrushing rinse (43). Effects on gingivitis have not been reported. Additional long-term studies have questioned the efficacy of this product to reduce plaque and gingivitis.

The active ingredient is stated to be sodium benzoate. However, the product also has about 30% of some of the ingredients (oils) found in Listerine. It contains 7.5% alcohol. Usage is as a prebrushing rinse. It is not ADA accepted.

Quaternary Ammonium Compounds

Quaternary ammonium compounds have been evaluated in a number of short-term studies relative to their effect on plaque and gingivitis. In these studies, an average plaque reduction of 35% has been reported, with mixed effects on gingival health (44, 45). A 6-month study has been reported showing a 14% reduction in plaque and a 24% reduction in gingivitis (46). Cepacol®, Scope®, and Advanced Care Viadent™ are well-known representatives of this group, each with concentrations of approximately 0.05% cetylpyridium chloride. In addition, Scope contains 0.005% domiphen bromide. The mechanism of action is related to increased bacterial cell wall permeability, which favors lysis, decreased cell metabolism, and a decreased ability for bacteria to attach to tooth surfaces. These agents are categorized as being cationic, which favors their attraction to anionic surfaces of teeth and plaque. They are surface-active agents that alter surface tension and have some substantivity.

Adverse effects have been some tooth staining and a burning sensation in the oral cavity. These agents are available in a 14–18% alcoholic vehicle with a pH range of 5.5–6.5. Recommended usage is twice daily, and they are not ADA accepted.

Sanguinarine

Short-term studies of sanguinarine have shown some plaque and gingivitis reduction (47, 48). In the long-term studies of the product in a dentifrice form, no significant reduction in plaque or gingivitis occurred, with the exception of one study in which the product was used as a dentifrice and as a mouthrinse (49, 50).

The proposed mechanism of action is by alteration of bacterial cell surfaces so that aggregation and attachment is reduced.

Sanguinarine (benzophenathradine) is derived from the bloodroot plant (*Sanguinaria canadensis*). The extract concentration in the product is 0.03%, which equals 0.10% sanguinarine. It also contains 0.2% zinc chloride. The product may be cationic, and the degree of substantivity is unclear. Adverse effects have been a burning sensation and a question of epithelial cell dysplasia. It is available as Viadent toothpaste and Viadent mouthrinse. The mouthrinse pH is 4.5, the dentifrice pH is 4.8, and the alcohol content of the rinse is 11.5%. It is not ADA accepted.

Triclosan

Triclosan (2,4,4′-Trichloro-2′-hydroxdiphenyl ether) is a new antiplaque/antigingivitis agent available in dentifrices. The addition of a copolymer, vinylmethyl-ether maleic acid (Gantrez), has been shown to improve the effectiveness of triclosan by enhancing its retention (substantivity) by hard and soft surfaces. This formula (Colgate Total) has been approved by the FDA for sale in the United States, and is ADA accepted. Claims allowed are for the reduction of plaque, gingivitis, calculus, and caries. Studies as early as 1973 showed that this chemical agent had a broad spectrum, antimicrobial effect against a wide range of gram-positive and gram-negative bacteria found in the mouth. The minimal concentration of triclosan for oral pathogens is 0.3 mg/ml. Triclosan's

antibacterial activity is not affected by anionic agents, such as lauryl sulfate, which are essential to dentifrice and mouthwash formulations—a fact that broadens its range of use. In doses lower than 0.5%, taste perception is minimally affected; however, at concentrations of greater than 0.5%, undesirable effects on taste occur.

Zinc citrate

This agent is found in some tartar control dentifrices and also has some plaque- and gingivitis-reducing properties as found in Mentadent® and Advanced Care Viadent®. ADA does not accept dentifrices with this ingredient for reducing plaque and gingivitis

MECHANICAL PRODUCTS FOR PLAQUE CONTROL

Good control of plaque is accomplished by mechanical procedures, which include brushing, flossing, and professional prophylaxis. A professional cleaning is recommended at least twice a year to remove plaque and tartar (calculus), both supragingivally and subgingivally.

Brushing

A recent survey of brushing habits in the United States showed that only 60% of the public follow a strict brushing regimen. Clearly, motivation and education are needed in this area.

For the average adult, a soft brush with rounded bristles is most efficient in removing plaque from supragingival tooth surfaces (with the exception of the surfaces between the teeth). Most bristles are made of nylon, and the bristle ends are rounded. Subgingival plaque can be removed only to a depth of a few millimeters. For patients with a highly developed gagging reflex, a child's toothbrush is recommended. In addition, these patients sometimes find that placing a small amount of salt on the tongue is helpful in checking the desire to gag.

Studies of toothbrushing methods indicate that thoroughness is more important than technique. In the United States, the most widely used technique is one in which the bristles are directed into the gingival crevice at a 45° angle, and a gentle, jab-jiggle action is used. The motion is elliptical, rather than a back-and-forth scrubbing. Power toothbrushes are of special value for people who have motor coordination problems or difficulty in properly removing plaque by manual brushing. For children, the novelty effect of the powered brush is sometimes of motivational value. Also, a number of studies have shown advantages of 10–15% better plaque removal than manual brushing.

Flossing

Surveys find that only 25% of the population questioned use dental floss regularly. Flossing is essential for removal of plaque from the surfaces between teeth and under the gumline, where the toothbrush does not reach. Because plaque has a propensity to build up in these areas, some dentists feel that flossing is actually more important than brushing.

Patients who do not have the manual dexterity to use dental floss can use the various types of dental floss holders or powered interdental cleaners (e.g., Braun Interclean and WaterPik Interdental Cleaner). Dental floss is available in waxed, lightly waxed, and unwaxed varieties. Most dentists feel that lightly waxed and unwaxed types are the most efficient in plaque removal. If the floss shreds or splits during use, this may be a sign of decay between the teeth or a defective filling margin. However, new flosses have been introduced that do not shred and are easier to use. The first of these new flosses was Glide Floss, followed by similar products from Colgate and Oral B®.

Disclosing Agents

Disclosing agents are dyes similar to those in food colorings that, when introduced into the oral cavity, color the supragingival plaque and make it easily visible. Various dyes are available in both liquid and tablet form. They are used in the dental office and at home both to increase the patient's awareness of plaque and to demonstrate where self-care has been ineffective in removing plaque.

Toothpastes

The majority of toothpastes advertised as specially formulated to control plaque contain (in addition to fluoride) a foaming agent and a mild abrasive, both of which facilitate plaque removal. However, the only toothpaste accepted by the ADA as possessing an active ingredient with proven ability to prevent or control plaque formation and reduce gingivitis is Colgate Total, with Triclosan as the active ingredient. Toothpastes claiming to be effective against plaque are simply more effective than brushing without any toothpaste because the use of toothpaste motivates people to brush longer and more thoroughly. In fact, it is mainly the mechanical action of brushing that removes plaque.

Toothpastes are effective as vehicles to deliver fluoride and Triclosan to the tooth surface, and although fluoride may have some effect against plaque bacteria and their enzymes, its major effect is to make the tooth surface more resistant to destruction by plaque bacteria. With the exception of Colgate Total, other toothpastes are accepted by the ADA for their fluoride content and effectiveness against tooth decay but not for their plaque–and gingivitis-reducing properties.

Other Oral Hygiene Aids

A number of devices aid in the removal of plaque from surfaces between teeth, around bridgework, and in other areas that are difficult to reach. The limitation of many of these devices is that they are effective for control of supragingival plaque but, at best, can remove subgingival plaque only to a depth of few millimeters. Therefore, they are of minimal value against subgingival plaque located deeper within the gingival crevice, as is the case in periodontal disease.

Various oral irrigators on the market remove some loosely attached plaque and particles of debris present around teeth and dental appliances, including braces (51). Because they are not effective in removing all attached plaque, they are not substitutes for brushing and flossing; rather, they should be used as adjuncts to these procedures (52). In addition, oral irrigators are limited in their ability to reach subgingival plaque. However, the introduction of subgingival applicator tips allows solutions to be delivered 6–7 mm apically.

Some studies have suggested that irrigators may alter plaque composition by eluting bacterial endotoxins (53). Patients with severely inflamed gum tissues should be cautioned to use irrigators at low pressures to guard against tissue laceration (if the tissue is severly inflammed), which may aggravate the existing problem.

Tartar (Calculus)-Reducing Products

A number of products, both dentifrices and mouthrinses, are available for reduction of supragingival calculus (tartar) in dental patients (54, 55). Calculus reduction has been shown with dentifrices containing pyrophosphates, zinc salts, triclosan, and papain.

The incidence of calculus formation ranges from 45 to 66%, with some variation between males and females and different age groups. Although supragingival calculus is not a major etiologic agent for gingivitis or periodontitis, its surface porosity provides an environment for plaque formation. In addition, it serves as a plaque-delivery system by holding plaque against gingival tissues. Although plaque formation has been well correlated with gingivitis and periodontitis, a similar correlation for calculus has not been reported. For this reason, the ADA does not offer an acceptance program for products that reduce calculus formation because this is considered to be a cosmetic issue, rather than an issue of disease.

The mechanism of action of the calculus-reducing chemicals is related to the latter's ability to inhibit crystal growth and interrupt the transformation of calcium phosphate (found in foods and saliva) into dental calculus. This effect may occur as follows:

1. The agents complex on the tooth surface to block receptor sites for calcium phosphate that precipitates from saliva and chemically absorbs to initiate calculus formation.
2. This same receptor site blockage also occurs in the calculus matrix as it begins to form.
3. The pyrophosphate complexes combine with free calcium in saliva to inhibit the attachment at the tooth surface (probably a secondary mechanism).

Because these products offset mineralization, there has been concern over demineralization of teeth. All manufacturers have addressed this issue and have reported that this has not been a problem, probably because of the positive effect of fluoride on remineralization of dentin and enamel.

Some patients cannot use tartar control toothpastes containing pyrophosphates because they develop tooth sensitivity and sloughing of tissue (56). These adverse effects have not been reported with nonpyrophosphate-containing tartar control products such as those made by Den-Mat Corporation (Rembrandt® Toothpaste).

Crest tartar control dentifrice

This dentifrice contains 3.4% tetrasodium pyrophosphate and 1.37% disodium dihydrogen pyrophosphate to reduce calculus. Also, 0.243% sodium fluoride is included for caries reduction and prevention. It was the first calculus-reducing dentifrice introduced into the United States. On the basis of various clinical studies, a reduction of 30–40% can be expected. It has also been shown to significantly reduce the tooth staining seen in some patients who use chlorhexidine.

Crest tartar control mouthrinse

This mouthrinse provides 1.6% ionic pyrophosphate from disodium and tetrasodium pyrophosphate to act against calculus formation and 0.05% sodium fluoride as a

caries-reducing agent. Data on the extent of calculus and caries reduction were not available when this article was written because the product was in test market.

Colgate tartar control dentifrice

This product contains 5% tetrasodium pyrophosphate and a polymeric fatty acid with the company-patented name of Gantrez as the calculus-reducing agents. Also, 0.243% sodium fluoride is included for caries reduction and prevention. On the basis of various clinical studies, a calculus reduction of 35–50% can be expected. It is equal to Crest in terms of calculus reduction, with some clinical studies even suggesting a superiority to Crest.

Colgate tartar control mouthrinse

This mouthrinse contains tetrasodium pyrophosphate and tetrapotassium pyrophosphate, which provide 1% ionic pyrophosphate. It also contains 0.02% fluoride. Calculus reduction has been reported to be 35–40% with twice-a-day rinsing, with no claim made for caries reduction.

Listerine tartar control mouthrinse

This mouthrinse contains 0.09% zinc chloride to reduce calculus and also contains the same ingredients as Listerine mouthrinse.

Rembrandt mouth-refreshing rinse

This product has been shown to reduce tartar due to a formulation of surface-active agents and citroxain, a form of papain.

Targon®

This mouthrinse reduces staining due to a formulation of surface-active agents. With the introduction of these products, the practitioner is offered a variety of dosage forms and flavors. If one decides to recommend a calculus-reducing agent, the product selection should be based on the product the patient likes to use best and one that will not diminish his awareness of the importance of plaque control. For example, if he is not already using a mouthrinse, would its introduction de-emphasize the mechanical methods of brushing and flossing as a means of plaque and/or calculus reduction?

HALITOSIS

Local factors, systemic factors, or a combination of both can cause halitosis. It is estimated that 80% of all mouth odors are caused by local factors within the oral cavity, and these odors are most often associated with caries, gingivitis, and periodontitis. Oral malodors occur because of the action of various microorganisms on proteinaceous substances, such as, exfoliated oral epithelium, salivary proteins, food debris, and blood (57, 58).

Studies have shown that saliva from individuals who are free of dental disease produces malodor less rapidly than saliva from patients with dental disease. It has also been observed that after prolonged periods of decreased salivary flow and abstinence from food and liquid malodors tend to be most severe.

Various oral bacteria produce products that are degraded to a number of compounds, foremost of which are sulfides and mucoproteins (59). These compounds have been most often associated with oral malodor. Specifically, it appears that oral malodor usually results from the bacterial-mediated degradative processes of methyl mercaptan and hydrogen sulfide in oral air. Ammonia is also produced but does not appear to contribute significantly to halitosis. It has even been suggested that ammonia production may improve the odor of mouth air.

Control of halitosis is directed at its etiology. If systemic factors are the problem, a medical consultation is indicated. If local factors are responsible, efforts should be directed toward their elimination. However, for many patients, systemic or local factors cannot be identified. Tongue scraping has been shown to reduce malodor in some patients.

Mouthwashes and dentifrices can serve an esthetic function by reducing halitosis. They can accomplish this by masking malodors, acting as antimicrobial agents, or both. There are no ADA-accepted products to reduce halitosis at this time.

TOPICAL ANESTHETICS

Topical anesthetic agents are selected for their ability to diffuse into the oral mucosa. Because many anesthetics used effectively for nerve block or infiltration do not adequately cross the mucosa, they cannot be used for topical anesthesia.

The concentration of anesthetic used for surface application is 2–5%. The rate of onset of topical anesthesia ranges from 2 to 5 min, is of relatively short duration, and has minimal effects deep to the area of application. One exception is a mucosal patch containing 10.4 mg of Lidocaine that gives anesthesia deep into the gingiva after a 5-min application period. Systemic absorption of topical anesthetics applied to the oral

mucosa is rapid, and blood levels may approach those seen following injection (60).

Several drugs used as topical anesthetics are not readily soluble in water but are soluble in organic solvents. They are, thus, prepared in alcohol, propylene glycol, polyethylene glycol, volatile oils, and other vehicles suitable for surface application. Their slower absorption rates make them safer for topical use on abraded or lacerated tissue. They produce anesthesia for short periods.

Topical anesthetics are useful to temporarily relieve the pain of ulcers, wounds, and other injured areas. The topical use of anesthetic agents before injection may produce superficial anesthesia. They are also of value in taking impressions or intraoral radiographs in patients with an excessive gag reflex.

Patients who are allergic to parenterally administered local anesthetics will also be allergic to topical application of these agents. In addition, as the agents may be absorbed into the systemic circulation, careless application of excessive amounts can result in signs of systemic toxicity. Symptoms of toxicity should be treated, as they would be for injectable agents. One can minimize the absorption of these agents by limiting the concentration of the drug, the area of application, and the total amount applied. In general, for topical anesthesia, one should use no more than one-fourth to one-half the maximum recommended dosage for injection of the agent.

Some topical anesthetic preparations are marketed in spray containers. These containers make it difficult to control the amount of material expelled and to confirm the agent was applied to the desired site. If these agents are applied to the posterior part of the mouth, a patient may inhale enough of the aerosol spray to provoke a toxic reaction (61). Use of topical anesthetics on the posterior pharynx may alter the swallowing reflex.

Benzodent

This ester-type anesthetic is poorly absorbed. Because it contains benzocaine, which has a low water solubility, it is prepared in a base containing petrolatum and sodium carboxymethylcellulose. Eugenol is included for its antiseptic and anodyne properties. Hydroxyquinoline sulfate is a preservative. This ointment can be directly applied to abraded or ulcerated lesions with minimal systemic effects. It is sometimes used to temporarily relieve denture sores and painful lesions.

Hurricaine

This ester-type anesthetic also contains benzocaine and is prepared in a polyethylene glycol base with flavoring agents added. It is available as a liquid, gel, or spray. The propellant for the spray is A 70.

Butyn

This ester-type anesthetic contains butacaine, with benzyl alcohol as a preservative. It is available as an ointment. The maximum dose is 5 ml of a 4% solution or 200 mg.

Cetacaine

This ester-type anesthetic is a combination of tetracaine HCl (2%), butyl aminobenzoate (2%), and benzocaine (14%). Benzalkonium chloride and cetyl dimethylammonium bromide are included as surface-active agents to facilitate the passage of benzocaine into the mucosal tissues.

Tetracaine is rapidly absorbed through biologic membranes and requires no facilitating agents. Because of its high toxicity and absorption, agents containing tetracaine should be used with caution and should not be placed under dentures. Spraying this agent is dangerous because the patient may inhale the aerosol. The maximum amount to be applied is 20 mg or 1 ml of a 2% solution. Cetacaine is available as a liquid, ointment, spray, or gel.

Xylocaine

This amide-type anesthetic contains a lidocaine base in a monoaqueous vehicle. It is available as a 2% viscous product containing lidocaine 2%, sodium carboxymethylcellulose, sodium saccharin, methylparaben, propylparaben, flavors, and purified water. It is also available as a liquid containing 4% methylparaben, sodium hydroxide, and flavoring agents. Another dosage form is a 5% ointment containing lidocaine 5%, polyethylene glycol, propylene glycol, and flavoring. The maximum dose is 300 ml of a 5% liquid form or 15 ml of the 2% viscous preparation.

DENTIFRICES AND SENSITIVE TEETH

Sometimes a patient will complain of teeth that are hypersensitive to heat and cold. These teeth usually have exposed root surfaces, sometimes with a loss of cementum. Most teeth, when in an ideal position in the mouth, have only the enamel surface exposed to the oral cavity. On occasion, such teeth may even respond with pain to extreme heat or cold.

However, in true dentinal hypersensitivity, the response to thermal and tactile changes is more pronounced, sometimes eliciting severe pain. Root surface exposure that allows contact with stimuli may occur because of gingival recession or following periodontal therapy.

Several theories have been advanced to explain the mechanism of dentinal hypersensitivity (62): innervation of the dentinal tubules, permitting transmission of impulses to the pulp, or the presence of lymph fluid in the dentinal tubules. In the latter case, exposure of dentin results in increased colloidal pressure on the tubules (thereby increasing pressure on the odontoblastic cells). Also proposed is a hydrodynamic mechanism involving the movements of tubular fluid in either direction, which elicits pain in the nerves of the pulp. Although no one theory has been proved, occlusion of the dentinal tubules by various methods brings relief. Various dentifrices are recommended for the treatment of sensitivity, with some success.

The greatest success occurs with dentifrices containing 5% potassium nitrate (e.g., Sensodyne®, Rembrandt, Crest, AquaFresh®, and Protect®), and some fluoride-containing dentifrices. Recently, a dentifrice containing potassium nitrate and stannous fluoride has been introduced to treat this problem (Colgate).

The primary mechanisms postulated for these dentifrices are that they occlude dentinal tubules, preventing stimuli from the oral cavity from irritating the dental nerve via these tubules. Also, those containing potassium may depolarize nerve fibers resulting in decreased impulse conduction and an associated decrease in pain.

For maximum effect, a patient must use only one of these dentifrices for at least a month. If no benefit occurs after a month, a different dentifrice should be recommended or other methods employed.

Topical varnishes containing sodium fluoride have also been shown to reduce dentinal hypersensitivity (e.g., Duraphat and Fluor-Protect) as well as reduce root surface caries.

BLEACHING AGENTS

Tooth-bleaching agents can be classified as to whether they are used for external or internal bleaching and whether the procedure is performed in the office by a dentist or at home by a patient. For tooth bleaching, hydrogen peroxide (H_2O_2) is used alone at levels of 30% or at 10–22% levels in a stable gel of carbamide peroxide (urea peroxide) that breaks down to form hydrogen peroxide (3.35% H_xO_2 from 10% carbamide peroxide), urea, ammonia, and carbon dioxide. The FDA has not approved peroxide solutions for use as a home bleach, however.

Internal Bleaching

Internal bleaching produces reliable results when used to eliminate intrinsic stains in dentin caused by blood breakdown products or endodontics or for stains in receded pulp chambers. Internal bleaching is always an in-office procedure.

External Bleaching

External bleaching is indicated for teeth that are disclosed from aging, fluorosis, or staining due to the effects of tetracycline (63). External bleaching can be applied by the dentist or staff or can be applied by the patient in home-use bleaching. When dentist-administered and home-use bleaching are both used, it is called "dual bleaching."

Dentist-applied external bleaching can be done with periodic repetitions of an office-bleaching agent using Superoxol or 30% H_2O_2. An etching gel containing phosphoric acid applied to selected dark areas increases the penetration of the bleach. Light is used to produce heat, which accelerates the bleaching process. External bleaching may need additional treatment every 1–2 years to touch up relapses. Severely stained teeth may require more frequent retreatment.

Home bleaching, supervised by the dentist, is done by the patient at home using a custom-made carrier that holds the bleach against the patient's teeth (64). After the desired result is achieved, overnight use on a periodic basis (1–4× month) can maintain the lightening that has been achieved.

External bleaching is seldom permanent, lasting approximately 1–4 years, after which teeth gradually return to their original color. Usually the younger the patient, the longer the bleaching will last. The more difficult it is to bleach a tooth, the more likely it is to discolor again. Bluish–gray stains seem to reappear more quickly than yellow stains. Because reoccurrence of staining is unpredictable, promises about longevity should not be made. Internal bleaching usually lasts longer than external bleaching.

Whitening Formulas

Whitening of teeth can occur by two mechanisms. One method is mechanical, in which an abrasive is used to

remove debris from the tooth. The other method involves either the use of peroxides, which react with water to form free oxygen radicals that help to whiten the teeth or a combination of mechanical and chemical actions. This latter mechanism is found with bleaching agents and is longer lasting than whitening procedures.

XEROSTOMIA

The widely held belief that saliva production significantly decreases with age is not well supported in the literature dealing with this subject. Aging does not appear to play a major role as a single contributing factor in causing xerostomia (65). However, senior citizens may receive medication that produces the side effect of xerostomia. The aged also develop medical problems that can diminish salivary production.

For these reasons, most of the studies of xerostomia have focused on older patients. One study reported a direct correlation between the intake of anticholingergic drugs, sedatives, and hypnotics and xerostomia (66). Over 400 drugs have been identified as potential reducers of salivary flow by acting on the cholinergic (parasympathetic) system either directly or indirectly (67). Another study found that the use of drugs producing xerostomia increases with age and, as expected, is highest in institutionalized patients. There are over 30 classifications of prescription and nonprescription medications that can reduce salivary flow.

Other factors that can cause xerostomia are systemic disorders and radiation (67). These factors must be considered in the differential diagnosis of xerostomia.

Clinical Problems with Xerostomia

Clinical problems associated with reduced salivary flow include difficulty chewing foods, reduced denture retention, recurrent caries, root surface caries, and oral candidiasis (low grade). When any of these conditions are found in a patient, regardless of age, reduced salivary flow should be considered in a differential diagnosis of the problem.

Treatment

Treatment of patients with reduced salivary flow should include the following: (1) drug and dosage changes by the patient's physician in consultation with the patient's dentist; (2) use of artificial saliva in a spray form; (3) use of mouth moisturizers and lip balms; (4) use of sugarless hard candy; (5) frequent sipping of water; (6) use of decaffeinated products; (7) use of pilocarpine (Salagen) 3–5× daily; and (8) inclusion of citrus and pineapple flavors in the diet.

LOCAL DELIVERY OF ANTIMICROBIAL AGENTS

In the past decade, significant research and product innovations have focused the attention of dental practitioners on the concept of the local application of antimicrobials to treat periodontal diseases. Three local delivery agents are now available in the United States, and two additional products are available in other parts of the world.

Though the rationale of antimicrobial approaches to treatment is evident, their limitations have also been evident. With systemic therapy, it may be difficult to achieve bacteriostatic or bactericidal antibiotic concentrations in pockets without using doses that evoke systemic side effects. The development of bacterial resistance is also an issue. The rise of antibiotic resistant, disease-producing bacterial strains is currently a major public health concern. Prolonged, repetitive courses of antibiotics for recurring dental infections is discouraged, because such practice can more readily lead to the development of resistance (68). Preferably, the cause of the infection should be eliminated rather than merely "managed" with antibiotics. Once antibiotic therapy is initiated, however, the importance of compliance with dosage and duration of treatment must be stressed with the patient. With poor patient compliance, under-dosing may occur, which, in turn, can favor the emergence of resistant bacteria.

Controlled Medication Delivery

The limitations of systemic therapy have prompted extensive research for the development of alternative delivery systems. Local, controlled delivery systems are available to release pilocarpine to the eye for a week after single placement for treatment of glaucoma. The oral cavity offers another relatively accessible disease site for localized therapy. In localized therapy for periodontal disease, the concern is the difficulty in reaching deep pockets and sustaining bacteriostatic or bactericidal levels long enough to be effective but not causing the development of resistance. The following is summary information about the various products available in the United States.

Tetracycline-containing fibers (Actisite®)

The first local delivery product available in the United States, one which has been extensively studied, is an ethylene–vinyl acetate copolymer fiber, diameter 0.5 mm, containing tetracycline, 12.7 mg/9 in. (Actisite tetracycline fiber; manufactured by Alza Corporation, Piscataway, NJ; distributed by Procter & Gamble Co., Cincinnati, OH; Fig. 1). When packed into a periodontal pocket, it is well tolerated by oral tissues, and for 10 days, it sustains tetracycline concentrations exceeding 1300 μg/ml, well beyond the 32–64 μg/ml required to inhibit the growth of pathogens isolated from periodontal pockets (69, 70). In contrast, crevicular fluid concentrations of only 4–8 μg/ml are reported following systemic tetracycline administration, 250 mg, 4× daily for 10 days (total oral dose, 10 g; 68). Thus, controlled site-specific tetracycline delivery can achieve a bactericidal effect at approximately 1/1000th of the dose administered systemically.

Studies demonstrate that the tetracycline fibers, applied with or without scaling and root planing, reduce probing depth, bleeding on probing, and periodontal pathogens and provide gains in clinical attachment level. Such effects are significantly better than those attained with scaling and root planing alone or with placebo fibers. The fibers used in conjunction with scaling and root planing have also provided a statistically significant improvement in probing depth reduction and clinical attachment level gains of over 60% and in bleeding on probing reductions over scaling and root planing alone at 6 months after therapy (71).

Actisite was the first local delivery system cleared by the FDA for the adjunctive treatment of recurrent periodontal disease. Although 6-month studies have demonstrated their value, longer-term studies are needed.

Chlorhexidine delivery system (PerioChip®)

A newer development in controlled local delivery, one that utilizes the antiseptic chlorhexidine as the antimicrobial agent, has been introduced in a number of countries and was recently cleared by the FDA for use in the United States. This delivery system, PerioChip (manufactured by Perio Products Ltd., Jerusalem, Israel; distributed by Dexell Pharmaceuticals, Edison, NJ), was developed in Israel and has been tested in the United States as well as in Europe.

The PerioChip is a small chip (4.0 × 5.0 × 0.35 mm) composed of a biodegradable hydrolyzed gelatin matrix into which has been incorporated 2.5 mg chlorhexidine gluconate per chip. It is rounded on one end and inserts easily and in less than a minute into periodontal pockets that are 5 mm or greater in depth. The PerioChip releases chlorhexidine and maintains drug concentrations in the gingival crevicular fluid greater than 100 μg/ml for at least 7 days, concentrations well above the tolerance of most oral bacteria (72). Because the PerioChip biodegrades in 7–10 days, a second appointment for removal is not needed. Studies with the PerioChip were as long as 9 months (73). At 9 months, significant decreases were observed in probing depth from baseline favoring the active chip plus scaling and root planing compared with controls (scaling and root planing only): chlorhexidin chip plus scaling and root planing, -0.95 ± 0.05 mm; placebo chip plus scaling and root planing, -0.69 ± 0.05 mm ($p = 0.00056$); scaling and root planing alone -0.65 ± 0.05 mm ($p = 0.00001$). The proportion of pocket sites with a probing depth reduction of 2 mm or more was increased in the chlorhexidine chip group compared with scaling and root planing alone, a difference which was statistically significant on a per patient basis ($p < 0.0001$). Improvements favoring the chlorhexidine chip compared with controls were also observed for clinical attachment levels at 9 months, improvements that were significant when the data were pooled ($p < 0.05$). Bleeding on probing was reduced in the active chip group compared with both controls, differences which were significant in one of the two studies ($p < 0.05$) and when the data were pooled ($p = 0.012$).

The results of these studies suggest that the Perio Chip may be a valuable adjunct to scaling and root planing in the treatment of periodontal disease. This product is easily placed, requires no appointment for removal, and provides reductions in probing depths similar to subgingivally placed antibiotics now available in various countries across the world. In addition, a major advantage of this system is that its active agent is an antiseptic instead of an antibiotic.

Subgingival Delivery of Doxycycline (Atridox®)

Atridox (manufactured by Atrix Laboratories, Fort Collins, CO) is a recently developed gel system that incorporates the antibiotic doxycycline (10%) in a syringeable gel system. An animal study in beagle dogs initially suggested some benefit to locally delivered doxycycline (74), and it is used in the veterinary population.

A recent 9-month, multicenter study was designed to study the effects of subgingivally placed doxycycline compared to subgingival placement of the vehicle and an herbal agent (Sanguinaria; 75). No scaling or root planing was performed in any of the groups, and there was no untreated group. The patients were instructed in oral

hygiene and randomly assigned to one of three groups: vehicle control, 5% sanguinarine in the vehicle control, and 10% doxycycline in the vehicle control.

Treatment with doxycycline was more effective than the other treatments at all time periods, with the exception of the 3-month clinical attachment level value. Also, when the authors evaluated the effect based on initial probing depth, the differential effect in the doxycycline group in comparison with the other two groups was greater as pretreatment probing depth increased. For the doxycycline group, the reduction in clinical attachment level at 9 months showed a gain of 0.4 mm compared to vehicle control, the reduction in probing depth was 0.6 mm greater than vehicle control, and the reduction of bleeding on probing was 0.2 units greater than vehicle control. Although the differences were small, they were statistically significant. The patient's oral hygiene scores (plaque index) averaged between 0.7 and 1.1 in all three groups throughout the study. Although resistance was not evaluated in this study, the local application of doxycycline has previously been reported to show transient increases in resistance in oral microbes and no overgrowth of foreign pathogens (76).

Data have recently been presented from two multicenter clinical trials (77). All treatment groups showed clinical improvements from baseline over the 9-month period. The results for all parameters measured were significantly better in the doxycycline group compared with vehicle control and oral hygiene only. Compared with scaling and root planing, the effects of doxycycline on clinical attachment level gain and probing depth reduction were equivalent.

Clinical study results suggest a potential periodontal benefit from the subgingival application of doxycycline. However, the value of this agent as an adjunct to scaling and root planing is untested. This product is cleared by the FDA for use in animals and humans.

HOST MODULATION

In 1998, the first nonantimicrobial drug to treat periodontal disease, Periostat, was approved by the FDA. Nonetheless, in the antibiotic family, the dose of the drug used is too low to kill bacteria. Periostat acts through its effects on inhibition of metalloproteinases, such as, collagenase and gelatinase. The therapeutic objective is to modulate the inflammatory host response. Periostat, available as a 20 mg capsule of doxycycline hyclate, is prescribed for use by patients twice daily. The mechanism of action is by suppression of the activity of collagenase, particularly that produced by polymorphonuclear leukocytes. Although this drug is in the antibiotic family, it does not produce any antimicrobial effects because the dose of 20 mg twice daily is too low to affect bacteria. As a result, resistance to this medication cannot develop.

Four double-blind, clinical, multicenter studies in over 650 patients have demonstrated that Periostat improves the effectiveness of professional periodontal care and slows the progression of the disease process (78).

REFERENCES

1. Maier, F.J. *Manual of Water Fluoridation Practice*; McGraw-Hill: New York, 1963; 48–59.
2. Brudevold, F.; Gardner, D.E.; Smith, F.A. Distribution of Fluoride in Human Enamel. J. Dent. Res. **1956**, *35*, 420–429.
3. Tinanoff, N.; Brady, J.M.; Gross, A. The Effect of NaF and SnF2 Mouthrinses on Bacterial Colonization of Tooth Enamel: TEM and SEM Studies. Caries Res. **1976**, *10*, 415–426.
4. Horowitz, H.S.; Heifetz, S.B.; Meyers, R.J.; Driscoll, W.S.; Korts, D.C. Evaluation of a Combination of Self-Administered Fluoride Procedures for the Control of Dental Caries in a Nonfluoride Area: Findings After Four Years. JADA **1979**, *98* (2), 219–223.
5. Council on Dental Therapeutics, American Dental Association. JADA **1975**, *91*, 1250–1251.
6. Newbrun, E. Current Regulations and Recommendations Concerning Water Fluoridation, Fluoride Supplements, and Topical Fluoride Agents. J. Dent. Res. **1992**, *71* (5), 1255–1265.
7. Levy, S.M. Review of Fluoride Exposures and Ingestion. Commun. Dent. Oral. Epidemiol. **1994**, *22* (3), 173–180.
8. DePaola, P.F.; Lax, M. The Caries-Inhibiting Effect of Acidulated Phosphate–Fluoride Chewable Tablets: A Two–Year Double-Blind Study. JADA **1968**, *76*, 554–557.
9. Driscoll, W.S.; Heifetz, S.B.; Brunnelle, J.A. Treatment and Posttreatment Effects of Chewable Fluoride Tablets on Dental Caries: Findings after $7\frac{1}{2}$ Years. JADA **1979**, *99* (5), 817–821.
10. Glenn, F.B. Immunity Conveyed by Sodium-Fluoride Supplement During Pregnancy: Part II. ASDC J. Dent. Child. **1979**, *46* (1), 17–24.
11. Glenn, F.B. Immunity Conveyed by a Fluoride Supplement during Pregnancy. ASDC J. Dent. Child. **1977**, *44* (5), 391–395.
12. Ripa, L.W. A Critique of Topical Fluoride Methods (Dentifrices, Mouthrinses, Operator- and Self-Applied Gels) in an Era of Decreased Caries and Increased Fluorosis Prevalence. J. Public Health Dent. **1991**, *51* (1), 23–41.
13. Ripa, L.W. Review of the Anticaries Effectiveness of Professionally Applied and Self-applied Topical Fluoride Gels. J. Public Health Dent. **1989**, *49* (5), 297–309.
14. Segal, A.H.; Stiff, R.H.; George, W.A.; Picozzi, A. Cariostatic Effect of a Stannous Fluoride-Containing Dentifrice on Children: Two-Year Report of a Supervised

Toothbrushing Study. J. Oral Ther. Pharmacol. **1967**, *4* (3), 175–180.
15. Keyes, F.M.; Overton, J.J.; McKean, T.W. Clinical Trials of Caries Inhibiting Dentifrices. JADA **1961**, *63*, 189–193.
16. DePaola, P.F.; Soparkar, P.; Foley, S.; Bookstein, F.; Bakhos, Y. Effect of High-Concentration Ammonium and Sodium Fluoride Rinses on Dental Caries in School-Children. Commun. Dent. Oral Epidemiol. **1977**, *5* (1), 7–14.
17. Reed, A.J.; Bibby, B.G. Preliminary Report on Effect of Topical Applications of Titanium Tetrafluoride on Dental Caries. J. Dent. Res. **1976**, *55* (3), 357–358.
18. Koch, G. Long-term Study of Effect of Supervised Toothbrushing with a Sodium Fluoride Dentifrice. Caries Res. **1970**, *4* (2), 149–157.
19. Koch, G. Comparison and Estimation of Effect on Caries of Daily Supervised Toothbrushing with a Dentifrice Containing Sodium Fluoride and a Dentifrice Containing Potassium Fluoride and Manganese Chloride. A Three-Year Clinical Test. Odontol. Rev. **1972**, *23* (3), 341–354.
20. Peterson, J.K. A Supervised Brushing Trial of Sodium Monofluorophosphate Dentifrices in a Fluoridated Area. Caries Res. **1979**, *13* (2), 68–72.
21. James, P.M.; Anderson, R.J.; Beal, J.F.; Bradnock, G. A 3-Year Clinical Trial of the Effect on Dental Caries of a Dentifrice Containing 2% Sodium Monofluorophosphate. Commun. Dent. Oral Epidemiol. **1977**, *5* (2), 67–72.
22. Moller, I.J.; Holst, J.J.; Sörensen, E. Caries Reducing Effect of a Sodium Monofluorophosphate Dentifrice. Br. Dent. J. **1968**, *124* (5), 209–213.
23. Gish, C.W.; Muhler, J.C.; Howell, C.L. Self Application of Fluoride as a Community Measure. J. Dent. Child. **1962**, *29*, 65–71.
24. Ripa, L.W.; Leske, G.S.; Sposato, A.; Varma, A. Effect of Prior Toothcleaning on Biannual Professional APF Topical Fluoride Gel-Tray Treatments. Results after Two Years. Clin. Prevent. Dent. **1983**, *5* (4), 3–7.
25. Houpt, M.; Koenigsberg, S.; Shey, Z. The Effect of Prior Toothcleaning on the Efficacy of Topical Fluoride Treatment. Two-Year Results. Clin. Prevent. Dent. **1983**, *5* (4), 8–10.
26. Brandt, R.S.; Slack, G.L.; Waller, D.F. The Use of a Sodium Fluoride Mouthwash in Reducing the Dental Caries Incresent in Eleven-Year-Old English School Children. Proc. Br. Paedoc. Soc. **1972**, *2*, 23–25.
27. Rugg-Gunn, A.J.; Holloway, P.J.; Davies, T.G. Caries Prevention by Daily Fluoride Mouthrinsing. Report of a Three-Year Clinical Trial. Caries Br. Dent. J. **1973**, *135* (8), 353–360.
28. Ripa, L.W.; Leske, G.S.; Sposato, A.L.; Rebich, T., Jr. Supervised Weekly Rinsing with a 0.2% Neutral NaF Solution: Results of a Demonstration Program after Four School Years. JADA **1981**, *102* (4), 482–486.
29. Stephen, K.W. Fluoride Toothpastes, Rinses, and tablets. Adv. Dent. Res. **1994**, *8* (2), 185–189.
30. Hunter, G.C., Jr.; Barringer, M.; Spooner, G. Analysis of Desensitization of Dentin by Sodium Silico-Fluoride and Gottliebis Solution. J. Periodontol. **1961**, *32*, 333–337.
31. Kanouse, M.C.; Ash, M.M., Jr.; Löe, H.; Schiott, C.R. The Effectiveness of a Sodium Monofluorophosphate Dentifrice on Dental Hypersensitivity. J. Periodontol. **1969**, *40* (1), 38–40.
32. Löe, H.; Schiott, C.R. The Effect of Mouthrinses and Topical Application of Chlorhexidine on the Development of Dental Plaque and Gingivitis in Man. J. Periodontal. Res. **1970**, *5* (2), 79–83.
33. Grossman, E.; Reiter, D.; Sturzenberger, O.P.; De la Rosa, M.; Dickinson, T.D.; Fenetti, G.A. Six Months Study of the Effects of a Chlorhexidine Mouthrinse on Gingivitis in Adults. J. Periodontal. Res. **1986**, *16* (Suppl.), 33, 34.
34. Segreto, V.A.; Collins, E.M.; Beiswanger, B.B.; De la Rosa, M.; Isaacs, R.L.; Lang, N.P. A Comparison of Mouthrinses Containing Two Concentrations of Chlorhexidine. J. Periodontal. Res. **1986**, *21* (Suppl.), 23–32.
35. Tinanoff, N.; Hock, J.; Camosci, D.; Helldén, L. Effect of Stannous Fluoride Mouthrinse on Dental Plaque Formation. J. Clin. Periodontol. **1980**, *7* (3), 232–241.
36. Tolle, S.L.; Bauman, D.B.; Allen, D.S. Effects of Fluoride Gels on Plaque and Gingival Health. Dent. Hyg. (Chic.) **1987**, *61* (6), 280–284.
37. Wolff, L.F.; Pihlstrom, B.L.; Bakdash, D.M.; et al. *Program and Abstracts, International Association for Dental Research*; Montreal Canada, March 1988, (abstract).
38. Weitzman, S.A.; Weitberg, A.B.; Stossel, T.P.; Schwartz, J.; Shklar, G. Effects of Hydrogen Peroxide on Oral Carcinogenesis in Hamsters. J. Periodontol. **1986**, *57* (11), 685–688.
39. Rees, T.D.; Orth, C.F. Oral Ulcerations With Use of Hydrogen Peroxide. J. Periodontol. **1986**, *57* (11), 689–692.
40. Fornéll, J.; Sundin, Y.; Lindhe, J. Effect of Listerine® on Dental Plaque and Gingivitis. Scand. J. Dent. Res. **1975**, *83* (1), 18–25.
41. Lamster, I.B.; Alfano, M.C.; Seiger, M.C. The Effect of Listerine® Antiseptic on Reduction of Existing Plaque and Gingivitis. Clin. Prev. Dent. **1983**, *5*, 12–16.
42. Gordon, J.M.; Lamster, I.B.; Seiger, M.C. Efficacy of Listerine® Antiseptic in Inhibiting the Development of Plaque and Gingivitis. J. Clin. Periodontol. **1985**, *12* (8), 697–704.
43. Emling, R.C.; Yankell, S.L. First Clinical Studies of a New Prebrushing Mouthrinse. Compend. Contin. Educ. Dent. **1985**, *6* (9), 636, 638–640, 644, 645.
44. Ciancio, S.G.; Mather, M.L.; Bunnell, H.L. Clinical Evaluation of a Quaternary Ammonium–Containing Mouthrinse. J. Periodontol. **1975**, *46* (7), 397–401.
45. Sturzenberger, O.P.; Leonard, G.J. The Effect of a Mouthwash as Adjunct in Tooth Cleaning. J. Periodontol. **1969**, *40* (5), 299–301.
46. Lobene, R.R.; Lobene, S.; Soparkar, P.M. The Effect of a Cetylpyridinium Chloride Mouthwash on Human Plaque and Gingivitis. J. Dent. Res. Prog. Abst. **1977**, *56*, 595.
47. Wennström, J.; Lindhe, J. Some Effects of a Sanguinarine-Containing Mouthrinse on Developing Plaque and Gingivitis. J. Clin. Periodontol. **1985**, *12* (10), 867–872.
48. Klewansky, P.; Vernier, D. Sanguinarine and the Control of Plaque in Dental Practice. Compend. Contin. Educ. Dent., S94–S97.
49. Lobene, R.R.; Soparkar, P.M.; Newman, M.B. The Effects of a Sanguinaria Dentifrice on Plaque and Gingivitis, Compend. Contin. Educ. Dent. **1986**, (Suppl. *7), S185–S188.*

50. Hanna, J.J.; Johnson, J.D.; Kuftinec, M.M. Six Month Evaluation of Sanguinarine Products in Orthodontic Patients. *Program and Abstracts, American Association of Dental Research*; Montreal Canada, March 1988, (abstract).
51. Elliott, J.R.; Bowers, G.M.; Clemmer, B.A.; Rovelstad, G.H. A Comparison of Selected Oral Hygiene Devices in Dental Plaque Removal. J. Periodontol. **1972**, *43* (4), 217–222.
52. Brady, J.M.; Gray, W.A.; Bhaskar, S.N. Electron Microscopic Study of the Effect of Water Jet Lavage Devices on Dental Plaque. J. Dent. Res. **1973**, *52* (6), 1310–1313.
53. Ciancio, S.G. New Evidence that Oral Irrigation Reduces Proinflammatory Proteins—Cytokines. Biological Therapies in Dentistry **1999**, *15*, 15–16.
54. Zacheral, W.A.; Pfeiffer, H.J.; Swancar, J.R. The Effect of Soluble Pyrophosphates on Dental Calculus in Adults. JADA **1985**, *110* (5), 737, 738.
55. Ciancio, S.G., Ed.; *ADA Guide to Dental Therapeutics*, 1st Ed.; American Dental Association: Chicago, 1999; 210–211.
56. Ciancio, S.G. Tartar Reduction without Pyrophosphates. Biological Therapies in Dentistry **1998**, (13).
57. Pitts, G.; Brogdon, C.; Hu, L.; Masurat, T.; Painotti, R.; Schumann, P. Mechanism of Action of An Antiseptic, Anti-odor Mouthwash. J. Dent. Res. **1983**, *62* (6), 738–742.
58. Tonzetich, J.; McBride, B.C. Characterization of Volatile Sulphur Production by Pathogenic and Non-Pathogenic Strains of Oral Bacteroides. Arch. Oral Biol. **1981**, *26*, 963–969.
59. Yaegaki, K.; Sanada, K. Volatile Sulphur Compounds in Mouth Air from Clinically Healthy Subjects and Patients with Periodontal. Disease. J. Periodontal. Res. **1992**, *27*, 233–238.
60. Gilman, A.G., Goodman, L.S., Gilman, A., Eds. *Goodman and Gilman's The Pharmaclogical Basis of Therapeutics*, 9th Ed.; Macmillan: New York, 1996.
61. Cianco, S.G., Ed. *ADA Guide to Dental Therapeutics,* 1st Ed.; American Dental Association: Chicago, 1999; 4–15.
62. Ciancio, S.G. Dentinal Hypersensitivity. Endodont. Dental Traumatol. **1986**, *12*, 150–152.
63. Albers, H.F. Lightening Natural Teeth. ADEPT Report **1991**, *2* (2), 1–24.
64. Haywood, V.B.; Leonard, R.H.; Nelson, C.F.; Brunson, W.D. Effectiveness, Side Effects and Long-Term Status of Nightguard Vital Bleaching. JADA **1994**, *125* (9), 1219–1226.
65. Sreebny, L.M.; Valdini, A. Xerostomia: A Neglected Symptom. Arch. Intern. Med. **1987**, *147*, 133–137.
66. Sreebny, L.M.; Schwartz, S.S. A Reference Guide to Drugs and Dry Mouth. Gerontology **1986**, *5*, 189–192.
67. Butt, G.M. Drug-Induced Xerostomia. J. Can. Dent. Assoc. **1991**, *57*, 391–393.
68. Gordon, J.M.; Walker, C.B.; Murphy, C.J.; Goodson, J.M.; Socransky, S.S. Tetracycline: Levels Achievable in Gingival Crevice Fluid and In Vitro Effect on Subgingival Organisms. Part I. Concentrations in Crevicular Fluid after Repeated Doses. J. Periodontol. **1981**, *52*, 609–612.
69. Tonetti, M.; Cugini, A.M.; Goodson, J.M. Zero Order Delivery with Periodontol. Placement of Tetracycline Loaded Ethylene Vinyl Acetate Fibers. J. Periodontal. Res. **1990**, *25*, 243–247.
70. Walker, C.B.; Gordon, J.M.; McQuilkin, S.J.; Niebloom, T.A.; Socransky, S.S. Tetracycline: Levels Achievable in Gingival Crevice Fluid and In Vitro Effect on Subgingival Organisms. Part II. Susceptibilities of Periodontal. Bacteria. J. Periodontol. **1981**, *52*, 613–616.
71. Newman, M.G.; Kornman, K.S.; Doherty, F.M. A 6-Month Multi-Center Evaluation of Adjunctive Tetracycline Fiber Therapy Used in Conjunction with Scaling and Root Planing in Maintenance Patients: Clinical Results. J. Periodontol. **1994**, *65*, 685–691.
72. Briner, W.W.; Kayrouz, G.A.; Chanak, M.X. Comparative Antimicrobial Effectiveness of a Substantive (0.12% Chlorhexidine) and a Nonsubstantive (Phenolic) Mouthrinse In Vivo and In Vitro. Compend. Contin. Educ. Dent. **1994**, *15*, 1158–1168.
73. Jeffcoat, M.K.; Bray, K.S.; Ciancio, S.G.; Dentino, A.R.; Fine, D.H.; Gordon, J.M.; Gunsolley, J.C.; Killoy, W.J.; Lowenguth, R.A.; Magnusson, N.I.; Offenbacher, S.; Palcanis, K.G.; Proskin, H.M.; Finkelman, R.D.; Flashner, M. Adjunctive Use of a Subgingival Controlled-Release Chlorhexidine Chip Reduces Probing Depth and Improves Attachment Level Compared With Scaling and Root Planing Alone. J. Periodontol. **1998**, *69*, 989–997.
74. Polson, A.M.; Southard, G.L.; Dunn, R.L.; Yewey, G.L.; Godowski, K.C.; Polson, A.P.; Fulfs, J.C.; Laster, L. Periodontal. Pocket Treatment in Beagle Dogs Using Subgingival Doxycycline from a Biodegradable System. I. Initial Clinical Responses. J. Periodontol. **1996**, *67*, 1176–1184.
75. Polson, A.M.; Garrett, S.; Stoller, N.H.; Bandt, C.L.; Hanes, P.J.; Killoy, W.J.; Southard, G.L.; Duke, S.P.; Bogle, G.D.; Drisko, C.H.; Friesen, L.R. Multi-Center Comparative Evaluation of Subgingivally Delivered Sanguinarine and Doxycline in the Treatment of Periodontitis. II. Clinical Results. J. Periodontol. **1997**, *68*, 119–126.
76. Larsen, T. Occurrence of Doxycycline-Resistant Bacteria in the Oral Cavity After Local Administration of Doxycycline in Patients with Periodontal. Disease. Scand. J. Infect. Dis. **1991**, *23*, 89–95.
77. Garrett, S.; Johnson, L.; Drisko, C.H.; Adams, D.F.; Bandt, C.; Beiswanger, B.; Bogle, G.; Donly, K.; Hallmon, W.W.; Hancock, E.B.; Hanes, P.; Hawley, C.E.; Kiger, R.; Killoy, W.; Mellonig, J.T.; Polson, A.; Raab, F.J.; Ryder, M.; Stoller, N.H.; Wang, H.L.; Wolinsky, L.E.; Evans, G.H.; Harrold, C.Q.; Arnold, R.M.; Southard, G.L.; et al. Two Multi-Center Studies Evaluating Locally Delivered Doxycycline Hyclate, Placebo Control, Oral Hygiene, and Scaling and Root Planing in the Treatment of Periodontitis. J. Periodontol. **1999**, *70*, 490–503.
78. Ciancio, S.; Ashley, R. Safety and Efficacy of Sub-Antimicrobial-dose Doxycycline Therapy in Patients with Adult Periodontitis. Adv. Dent. Res. **1998**, *12*, 27–31.